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(54) Title: MODIFIED SODIUM IODIDE SYMPORTER PROTEINS AND GENES FOR IMAGING AND CANCER THERAPY

(57) Abstract: The invention provides modified sodium iodide symporter (NIS) proteins, and polynucleotides encoding modified NIS proteins. The modified NIS proteins have a net electrostatic charge more positive than that of corresponding wild-type NIS proteins. Expression of a modified NIS protein in a cell results in higher intracellular concentrations of NIS substrates as compared to equivalent expression of the corresponding wild-type NIS protein in a cell. The invention also provides methods for imaging cells or for therapy of cancer cells, using the modified NIS proteins to facilitate transport of NIS substrates into cells in the body of an individual. Uptake of NIS substrates suitable for either imaging or that have cytotoxic activity, into the cells of the individual that express modified NIS protein facilitate detection of the substrate (for imaging) or killing of the cancer cells (for therapy).

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 15/00, 1/21, 15/11; C07H 21/04; C07K 14/00

US CL : 435/69.1, 252.3; 536/23.1, 23.5; 530/350

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/69.1, 252.3; 536/23.1, 23.5; 530/350

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6,391,579 B1 (CARRASCO et al) 21 May 2002 (21.05.2002), see columns 4-9.	25-33
Y		1-24
Y	HUANG. M. et al. Ectopic expression of the thyroperoxidase gene augments radioiodide uptake and retention mediated by the sodium iodide symporter in non-small cell lung cancer. 2001, Vol. 8, No. 8, pages 612-618, especially page 612 and 617, left column.	1-24, 29-32
Y	JHIANG. S. M. Regulation of Sodium/Iodide Symporter. Reviews in Endocrine and Metabolic Disorders. 2000, Vol. 1, pages 205-212, see especially page 205, right column and pages 213-214.	1-24, 29-32
Y	SHEN. D. H. Y. et al. Sodium Iodide Symporter in Health and Disease. Thyroid. May 2001, Vol. 11, No. 5, pages 415-425, see entire document.	1-33

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

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Continuation of B. FIELDS SEARCHED Item 3:

Medline, Biosis, EMBASE, Cancerlit, Biotechno CAPLUS, WEST.

Search terms: NIS, symporter, , radioiodide, iodide retention, iodination, modified and mutant NIS, inventor search